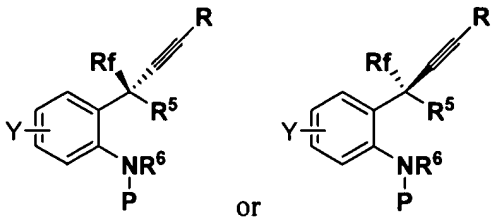
CLAIMS

WHAT IS CLAIMED IS:

1. A process for the asymmetric synthesis of the chiral compound of the structure



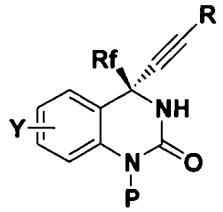
where Y is H, mono or multisubsubstituted electronwithdrawing group or electron-donating group, wherein Y can be located at *m*-,*o*-,or *p*-positon of the benzene ring;

P is hydgogen or an amino protecting group,

Rf is fluoro-containing alkyl,

R is trialkylsilyl, alkyl, cycloalkyl or aryl group,

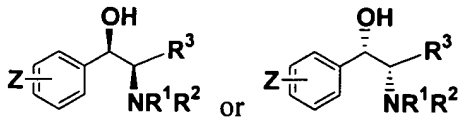
R^6 is hydrogen when R^5 is hydroxy, also $R^5$and R^6 can be –HNCO- of the structure or its enantiomer



where Y, P, R, Rf is the same as above;

Comprising the steps of:

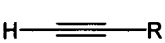
(a) providing a mixture of chiral ligand (1R, 2R)-2-*N*,*N*-substituted-1-(substituted -phenyl)-2-R^3-substituted-2-aminoethanol or its enantiomer, of the structure



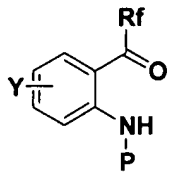
wherein R^1, R^2 is amino protecting group, and R^3 is alkyl; alkyl substituted with alkyloxy or

silyoxy, carboxylic group, carbalkoxy group, hydroxyl methyl, cycloalkyl , aryl or CH_2OR^4, wherein R^4 is an oxygen protecting group,

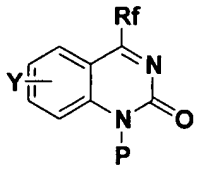
Z is H, mono or multisubsubstituted electronwithdrawing group or electron-donating group, wherein Z can be located at m-,o-,or p-positon of the benzene ring;

with a terminal alkyne and a Zn(II) , Cu(II) or Cu(I) salts in the presence of an organic base in aprotic solvent, wherein the terminal alkyne is  , R is the same as above,

(b) mixing with the mixture of step (a) of reactant of the structure



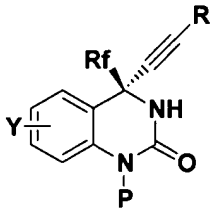
or of the structure



wherein P is hydrogen or an amino protecting group, Rf is fluoro-containing alkyl, Y is the same as above;

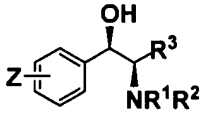
obtains the target addition product after normal isolation.

2. A process of claim 1, wherein the process is for the asymmetric synthesis of the chiral compound of the structure or its enantiomer



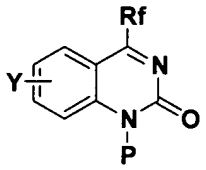
Comprising the steps of:

(a) providing a mixture of chiral ligand (1R, 2R)-2-*N*,*N*-substitutedamino-1-(substituted-phenyl)-2-substituted-2-aminoethanol, of the structure, or its enantiomer



with a terminal alkyne and a Zn(II) or Cu salts in the presence of an organic base in aprotic solvent, wherein the terminal alkyne is H—≡—R;

(b) mixing with the mixture of step (a) of reactant of the structure



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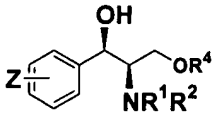
3. A process of claim 2, wherein the chiral ligand is (1R, 2R)-2-*N*,*N*-substitutedamino-1-(substituted-phenyl)-3-*O*-R^4substituted-propane-1-ol or its enantiomer,of the structure



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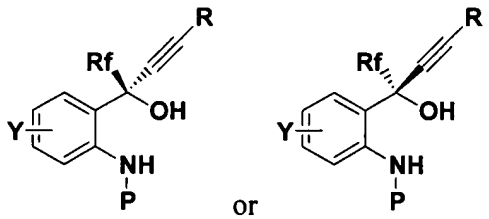
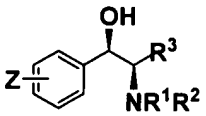
4. A process of claim 1, wherein the process is for the asymmetric synthesis of the chiral compound of the structure or its enantiomer



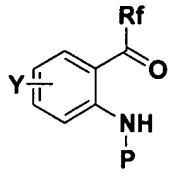
Comprising the steps of:

(a) providing a mixture of chiral ligand (1R, 2R)-2-*N*,*N*-substitutedamino-1-(substituted-phenyl)-2-R^3-substituted-1-ethanol or its enantiomer, of the structure ,



with a terminal alkyne and a Zn(II) or Cu salts in the presence of an organic base in aprotic solvent, wherein the terminal alkyne is H—≡—R;

(b) mixing with the mixture of step (a) of reactant of the structure



5. A process of claim 1, wherein R^1 and R^2 is alkyl, substituted alkyl, benzyl, trialkylsilyl or substituted benzyl, the substituted group can be phenyl, naphenyl, halo, nitro, hydroxy, C_1~C_3 hydroxyalkyl, C_1~C_4 alkyl, C_1~C_3 alkoxy; or R^1, R^2 can be $-(CH_2)_nX(CH_2)_m-$, where X can be CH_2, O or NH; n,m is an integer from 1 to 6.

   P is hydrogen, alkyl, substituted alkyl, benzyl, trialkylsilyl or substituted benzyl, the substituted group can be phenyl, naphenyl, halo, nitro, hydroxy;

   R^4 is alkyl, substituted alkyl, benzyl, trialkylsilyl or substituted benzyl, the substituted group can be phenyl, naphenyl, halo, nitro, hydroxy, C_1~C_3 hydroxyalkyl, C_1~C_4 alkyl, C_1~C_3 alkoxy or CN;

   electronwithdrawing group is halogen, NO_2, CF_3, CH_3SO_2, $CH_3CH_2SO_2$, $PhCH_2OCO$, or AcO. electron-donating group is alkoxy, OH, $Me_2NCH_2CH_2O$, $Et_2NCH_2CH_2O$, NH_2, C_1~C_4 alkyl.

6. A process of claim 1, wherein R^1 and R^2 is C_1~C_{20} alkyl , C_1~C_{20} substituted alkyl, trialkylsilyl , benzyl or substituted benzyl, the substituted group can be phenyl, naphenyl, halo, nitro, hydroxy, C_1~C_3 hydroxy alkyl, C_1~C_{20} alkyl, C_1~C_3 alkoxy; or R^1, R^2 can be $-(CH_2)_nX(CH_2)_m-$, where X can be CH_2, O or NH; n,m is an integer from 1 to 6;

   R^3 is C_1～C_{20} alkyl; C_1～C_{20} alkyl substituted with alkyloxy or silyoxy, carboxylic group, C_1-C_{20} carbalkoxy group, hydroxyl methyl, C_3～C_{20} cycloalkyl, aryl or CH_2OR^4, wherein R^4 is C_1~C_{20} alkyl, C_1~C_{20} substituted alkyl, benzyl or substituted benzyl, the substituted group can be phenyl, naphenyl, halo, nitro, hydroxy, C_1~C_3 hydroxyalkyl, C_1~C_4 alkyl, C_1~C_3 alkoxy or CN;

   Z is H, F, Cl, Br, I, CH_3SO_2, OH, $PhCH_2O$, AcO, MeO, EtO, $Me_2NCH_2CH_2O$, $Et_2NCH_2CH_2O$, $PhCH_2OCO$, *t*-Bu, *i*-Pr, NH_2, or NO_2

P is hydrogen, C_1~C_{20} alkyl, C_1~C_{20} substituted alkyl, benzyl, trialkylsilyl or substituted benzyl, the substituted group can be phenyl, naphenyl, halo, nitro, hydroxy, C_1~C_3 hydroxyalkyl, C_1~C_4 alkyl, C_1~C_3 alkoxy or CN;

Y is H, F, Cl, Br, I, CH_3SO_2, OH, $PhCH_2O$, AcO, MeO, EtO, $Me_2NCH_2CH_2O$, $Et_2NCH_2CH_2O$, $PhCH_2OCO$, *t*-Bu, *i*-Pr, NH_2, or NO_2

Rf is C_1～C_{20} fluoro-containing alkyl;

R is trialkylsilyl, C_1～C_{20} alkyl., C_3～C_{20} cycloalkyl or aryl group;

7. A process of claim 1, wherein R^1 and R^2 is C_1~C_4 alkyl , tri-phenylmethyl, *t*-butyldimethylsilyl, benzyl unsubstituted or substituted with C_1-C_4 alkyl; *para*-methoxy benzyl; *para*-nitrobenzyl; *para*-chlorobenzyl; 2, 4-dichlorobenzyl;2, 4-dimethoxybenzyl; or R^1, R^2 can be $-(CH_2)_2O(CH_2)_2-$, $-(CH_2)_2N(CH_2)_2-$, $-(CH_2)_5-$ or $-(CH_2)_6-$;

R^3 is C_1~C_4 alkyl, C_1~C_4 alkyl substituted with alkyloxy or silyoxy, carboxylic group, C_1~C_4 carbalkoxy group, hydroxyl methyl, C_3～C_6 cycloalkyl , aryl or CH_2OR^4, wherein R^4 is C_1~C_4 alkyl , tri-phenyl methyl, *t*-butyldimethylsilyl , benzyl unsubstituted or substituted with C_1~C_4 alkyl, *para*-methoxy benzyl, *para*-nitrobenzyl, *para*-chlorobenzyl, 2, 4-dichlorobenzyl, 2, 4-dimethoxybenzyl, or trialkylsilyl groups;

Z is H, F, Cl, Br, I, CH_3SO_2, OH, $PhCH_2O$, AcO, MeO, EtO, $Me_2NCH_2CH_2O$, $Et_2NCH_2CH_2O$, $PhCH_2OCO$, *t*-Bu, *i*-Pr, NH_2, or NO_2;

P is hydrogen , C_1~C_4 alkyl , tri-phenylmethyl, *t*-butyldimethylsilyl , benzyl unsubstituted or substituted with C_1~C_4 alkyl; *para*-methoxy benzyl, *para*-nitrobenzyl, *para*-chlorobenzyl, 2, 4-dichlorobenzyl, 2, 4-dimethoxybenzyl;

Y is H, Cl, Br, CH_3SO_2, $CH_3CH_2SO_2$, NO_2 or F;

Rf is C_1~C_4 fluoro-containing alkyl;

R is C_1~C_4 alkyl, C_3～C_6 cycloalkyl or aryl group, wherin aryl is phenyl, naphenyl, furan, thiophene , pyrrole;

Halogen or halo is fluoro, chloro, bromo and iodo.

8. A process of claim 1 ,wherein the stoichiometric ratios are about 0.1- 3 : 0.1-3 : 1-4 :1 of

ligand : Zinc salt:the organic base : substrate ketone or ketimine.

9. A process of claim 1 ,wherein the Zinc salt is selected from $ZnCl_2$, $ZnBr_2$, ZnF_2, ZnI_2, $Zn(OTf)_2$, $CuCl_2$, $CuBr_2$, $Cu(OTf)_2$, CuCl, CuBr, Cu(OTf).

10. A process of claim 1, wherein the organic base is selected from $MeN(iPr)_2$, $HNEt_2$, $N(iPr)_3$, pyridine, NEt_3, piperidine, $EtN(iPr)_2$, Bu_3N.

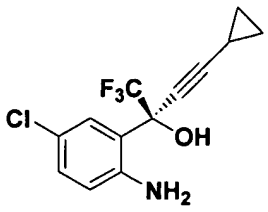
11. A process of claim 1, wherein the reaction temperature is 0-100°C

12. A process of claim 1, wherein the reaction temperature is 0-50°C.

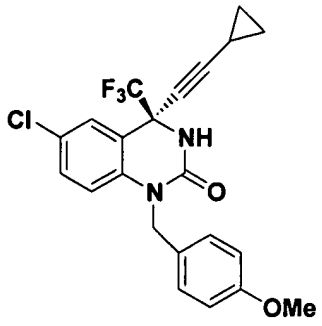
13. A process of claim 1, wherein the reaction solvent is selected from THF, dioxane, Et_2O, benzene, mono or multi-alkylsubstituted-benzene, DME, toluene, n-hexane, CH_2Cl_2 and cyclohexane, or mixture thereof. One preferred solvent is toluene.

14. A process of claim 1, wherein quenching the reaction by adding a proton source to give the desired compound.

15. A process of claim 1,wherein it is for the asymmetric synthesis of the chiral compound of the structure

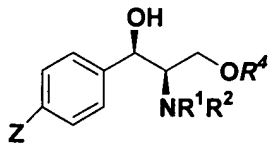


or of the structure



Comprising the steps of:

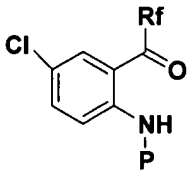
(a) providing a mixture of 0.1~3 molar equivalent of (1R,2R)-2-*N*,*N*-substitutedamino-1-(4-Z-substituted-phenyl)-3-*O*-R^4-*substituted* propane-1-ol, of the structure



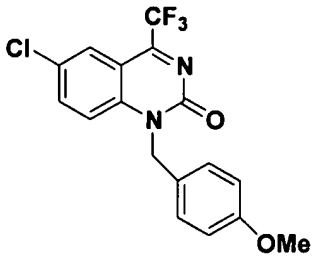
,

with 0.1~3 molar equivalent of cyclopropylacetylene and 0.1~3 molar equivalent of Zn(II), Cu(I)or Cu(II) salts and 1~4 molar equivalent of an organic base in organic solvent;

(b) mixing with the mixture of step (a) 1.0 molar equivalent of reactant of the structure



or of the structure

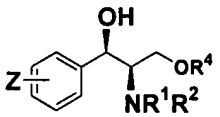


and maintaining the resulting reaction mixture at a temperature of between about 0-50°C for 1-20 hrs;

(c) quenching by adding a proton source ;

(d) to give the desired compound.

16. The compound of the structure or its enantiomer



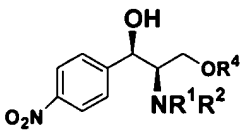
wherein R^1, R^2 is amino protecting group, and R^4 is oxygen protecting group; Z is mono or multisubstituted electronwithdrawing group or electron-donating group;

and when Z is NO_2 at 4-postion of the phenyl, R^1 is N=O, R^2 is $COCH_3$, R^4 is only alkyl, substituted alkyl, benzyl ,substituted benzyl, or trialkylsilyl;

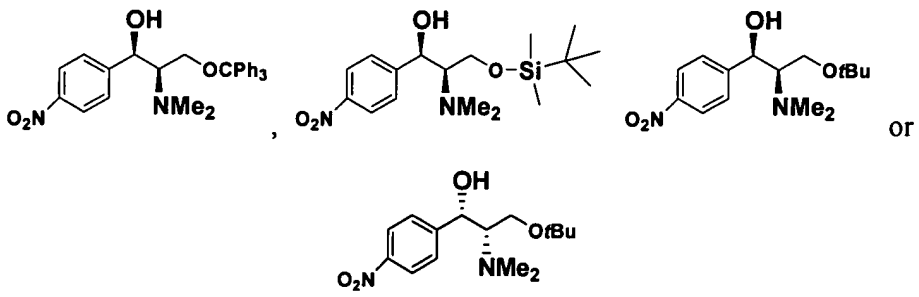
and when Z is NO_2 at 4-postion of the phenyl, R^1, R^2 is CH_3, the ligand is only (1R, 2R)-2-*N*,*N*-dimethylamino-1-(4- nitrophenyl)-3-*O*-R^4-1-propanol;

and when Z is OCH_3 at 4-postion of the phenyl, R^1, R^2 is CH_3, R^4 is only alkyl, substituted alkyl, benzyl ,substituted benzyl; said substituted group is phenyl , naphthyl, halogen , NO_2, hydroxyl, C_1~C_3 hydroxyalkyl, C_1~C_4 alkyl, C_1~C_3 alkoxy or CN;

17. The compound of claim 16, of the structure or its enantiomer



18. The compound of claim 16, of the structure or its enantiomer



19. The compound of claim 16, wherein R^1 and R^2 is alkyl , substituted alkyl , benzyl, trialkylsilyl or substituted benzyl, the substituted group can be phenyl, naphenyl, halo, nitro, hydroxy, C_1~C_3 hydroxyalkyl, C_1~C_4 alkyl, C_1~C_3 alkoxy; or R^1, R^2 can be $-(CH_2)_nX(CH_2)_m-$, where X can be CH_2, O or NH; n,m is an integer from 1 to 6;

R^4 is alkyl, substituted alkyl, benzyl or substituted benzyl, the substituted group can be phenyl, naphenyl, halo, nitro, hydroxy, C_1~C_3 hydroxy alkyl, alkyl, C_1~C_3 alkoxy or CN;

electronwithdrawing group is halogen, NO_2, CF_3, CH_3SO_2, $CH_3CH_2SO_2$, $PhCH_2OCO$ or AcO. electron-donating group is C_1~C_3 alkoxy, OH, $Me_2NCH_2CH_2O$, $Et_2NCH_2CH_2O$, NH_2, C_1~C_4 alkyl;

and when Z is NO_2 at 4-postion of the phenyl, R^1 is N=O, R^2 is $COCH_3$, R^4 is only alkyl, substituted alkyl, benzyl ,substituted benzyl, or trialkylsilyl;

and when Z is NO_2 at 4-postion of the phenyl, R^1, R^2 is CH_3, the ligand is only (1R, 2R)-2-*N*,*N*-dimethyl-1-(4- nitrophenyl)-3-*O*-R^4-1-propanol;

and when Z is OCH_3 at 4-postion of the phenyl, R^1, R^2 is CH_3, R^4 is only alkyl, substituted alkyl, benzyl, substituted benzyl.

20. The compound according to claim 16, wherein R^1 and R^2 is C_1~C_{20} alkyl , C_1~C_{20} substituted alkyl, trialkylsilyl, benzyl or substituted benzyl, the substituted group of alkyl or benzyl can be phenyl, naphenyl, halo, nitro, hydroxy, C_1~C_3 hydroxyalkyl, C_1~C_4 alkyl, C_1~C_3 alkoxy or CN; or R^1, R^2 can be $-(CH_2)_nX(CH_2)_m-$, where X can be CH_2, O or NH; n,m is an integer from 1 to 6;

R^4 is C_1~C_{20} alkyl, C_1~C_{20} substituted alkyl, benzyl, trialkylsilyl or substituted benzyl, the substituted group can be phenyl, naphenyl, halo, nitro, hydroxy, C_1~C_3 hydroxyalkyl, C_1~C_4 alkyl, C_1~C_3 alkoxy or CN;

Z is H, F, Cl, Br, I, CH_3SO_2 OH, $PhCH_2O$, AcO, MeO, EtO, $Me_2NCH_2CH_2O$, $Et_2NCH_2CH_2O$, $PhCH_2OCO$, *t*-Bu, *i*-Pr, NH_2, or NO_2;

and when Z is NO_2 at 4-postion of the phenyl, R^1 is $N{=}O$, R^2 is $COCH_3$, R^4 is only alkyl, substituted alkyl, benzyl,substituted benzyl, or trialkylsilyloxy;

and when Z is NO_2 at 4-postion of the phenyl, R^1, R^2 is CH_3, the ligand is only (1R, 2R)-2-*N*,*N*-dimethylamino-1-(4- nitrophenyl)-3-*O*-R^4-propane-1-ol;

and when Z is OCH_3 at 4-postion of the phenyl, R^1, R^2 is CH_3, R^4 is only alkyl, substituted alkyl, benzyl ,substituted benzyl; said substituted group is phenyl , naphthyl, halogen , NO_2, hydroxyl, C_1~C_3 hydroxyalkyl, C_1~C_4 alkyl, C_1~C_3 alkoxy or CN.

21. The compound according to claim 16, wherein R^1 and R^2 is C_1~C_4 alkyl , tri-phenyl methyl, *t*-butyldimethylsilyl, benzyl unsubstituted or substituted with C_1-C_4 alkyl; *para*-methoxy benzyl; *para*-nitrobenzyl; *para*-chlorobenzyl; 2, 4-dichlorobenzyl; 2, 4-dimethoxybenzyl;

R^4 is C_1~C_4 alkyl, tri-phenyl methyl, *t*-butyldimethylsilyl, benzyl unsubstituted or substituted with C_1~C_4 alkyl; *para*-methoxy benzyl; *para*-nitrobenzyl; *para*-chlorobenzyl; 2, 4-dichlorobenzyl; 2, 4-dimethoxybenzyl;

Z is H, F, Cl, Br, I, CH_3SO_2 OH, $PhCH_2O$, AcO, MeO, EtO, $Me_2NCH_2CH_2O$, $Et_2NCH_2CH_2O$, $PhCH_2OCO$, *t*-Bu, *i*-Pr, NH_2, or NO_2;

and when Z is NO_2 at 4-postion of the phenyl, R^1 is $N{=}O$, R^2 is $COCH_3$, R^4 is only alkyl, substituted alkyl, benzyl ,substituted benzyl, or trialkylsilyl;

and when Z is NO_2 at 4-postion of the phenyl, R^1, R^2 is CH_3, the ligand is only (1R, 2R)-2-*N*,*N*-dimethylamino-1-(4-nitrophenyl)-3-*O*-R^4-propane-1-ol;

and when Z is OCH_3 at 4-postion of the phenyl, R^1, R^2 is CH_3, R^4 is only alkyl, substituted alkyl, benzyl ,substituted benzyl.